The Locus of Cell Mechanisms

Schwann and the others in relating fermentation to the activity of living yeast cells: "Fermentation is correlated to the vital processes of yeast" (Pasteur, 1860, p. 323). For him and for many, this pointed to the futility of trying to provide a purely chemical account of fermentation. But despite Pasteur's influence, numerous researchers (e.g., Pierre Eugène Marcellin Berthelot, Moritz Traube, Felix Hoppe-Seyler) contended that it was a chemical constituent of yeast (as pepsin is a chemical substance in the stomach) that catalyzed the reaction. Wilhelm Kühne (1877a; 1877b) introduced the term *enzyme* (from "in yeast" in Greek), which eventually came to be the term in general use for such agents. Until Buchner's breakthrough in 1897 (discussed below), however, there was no compelling evidence that enzymes – that is, chemical agents – were responsible for fermentation. 28

During this period in which convincing empirical results supporting a chemical approach to fermentation were not forthcoming, chemically minded researchers focused on the mechanisms of animal respiration. Lavoisier's research had opened a prolonged conflict about whether respiration occurred in animals' lungs (Lavoisier), blood (Liebig, Bernard), or tissues (Pflüger). (For further discussion of this conflict, see Bechtel & Richardson, 1993, Chapter 3.) Eduard Pflüger (1872; 1875) ultimately provided compelling evidence that respiration occurred in the tissues. Settling this question opened the search for the mechanism within tissues that made respiration possible. Pflüger proposed that the protoplasm that comprised the cells of tissues had a complex physical structure that resulted from the polymerization of protein. He further proposed that this structure stored energy that could be released in "explosions" in the cell: "The life process is the intramolecular heat of highly unstable albuminoid molecules of the cell substance, which dissociate largely with the formation of carbonic acid, water, and amide-like substances, and

the viscous liquid: they die from indigestion caused by lack of exercise" (Wöhler, 1839; passage translated in Schlenk, 1997, p. 47).

²⁷ For Kühne the term marked a contrast between chemical agents and *organized ferments*, living organisms that produced chemical changes. The eventual use of the term *enzyme* for chemical agents thus reversed Kühne's intention in coining the term.

After Bernard's death in 1878 a manuscript was found in his country house proposing that alcoholic fermentation resulted from a soluble ferment found in ripe or rotting fruit (Bernard, 1878b). It was not clear whether Bernard was reporting actual results. This manuscript provoked Pasteur to pursue an extensive attempt to isolate such an enzyme and an extended exchange between Bertholet and Pasteur (For a review and discussion, see Friedmann, 1997; Kohler, 1971). About the same time, Marie Mikhailovna Manasseïn (1872) reported in the same journal in which Buchner was to publish that she had succeeded in producing fermentation in a cell-free extract. Her brief report, however, did not elicit much response.